

Avian influenza overview April – June 2023

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Avian influenza overview April – June 2023

European Food Safety Authority, European Centre for Disease Prevention and Control, European Union Reference Laboratory for Avian Influenza, Cornelia Adlhoch, Alice Fusaro, José L Gonzales, Thijs Kuiken, Angeliki Melidou, Gražina Mirinavičiūtė, Éric Niqueux, Karl Ståhl, Christoph Staubach, Calogero Terregino, Francesca Baldinelli, Alessandro Broglia and Lisa Kohnle

Abstract

Between 29 April and 23 June 2023, highly pathogenic avian influenza (HPAI) A(H5N1) virus (clade 2.3.4.4b) outbreaks were reported in domestic (98) and wild (634) birds across 25 countries in Europe. A cluster of outbreaks in mulard ducks for foie gras production was concentrated in Southwest France, whereas the overall A(H5N1) situation in poultry in Europe and worldwide has eased. In wild birds, black-headed gulls and several new seabird species, mostly gulls and terns (e.g. sandwich terns), were heavily affected, with increased mortality being observed in both adults and juveniles after hatching. Compared to the same period last year, dead seabirds have been increasingly found inland and not only along European coastlines. As regards mammals, A(H5N1) virus was identified in 24 domestic cats and one caracal in Poland between 10 and 30 June 2023. Affected animals showed neurological and respiratory signs, sometimes mortality, and were widely scattered across nine voivodeships in the country. All cases are genetically closely related and identified viruses cluster with viruses detected in poultry (since October 2022, but now only sporadic) and wild birds (December 2022–January 2023) in the past. Uncertainties still exist around their possible source of infection, with no feline-to-feline or feline-tohuman transmission reported so far. Since 10 May 2023 and as of 4 July 2023, two A(H5N1) clade 2.3.4.4b virus detections in humans were reported from the United Kingdom, and two A(H9N2) and one A(H5N6) human infections in China. In addition, one person infected with A(H3N8) in China has died. The risk of infection with currently circulating avian H5 influenza viruses of clade 2.3.4.4b in Europe remains low for the general population in the EU/EEA, low to moderate for occupationally or otherwise exposed people to infected birds or mammals (wild or domesticated).

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1. Introduction

This Scientific Report provides an overview of highly pathogenic avian influenza (HPAI) virus detections in poultry¹, captive² and wild birds as well as mammals, noteworthy outbreaks of low pathogenic avian influenza (LPAI) virus in poultry and captive birds, and human cases due to avian influenza virus that occurred in and outside Europe between 29 April and 23 June 2023.

The background, Terms of Reference and interpretation thereof are described in Appendix A, whereas the data and methodologies used are reported in Appendix B.

2. Assessment

2.1 HPAI virus detections in birds

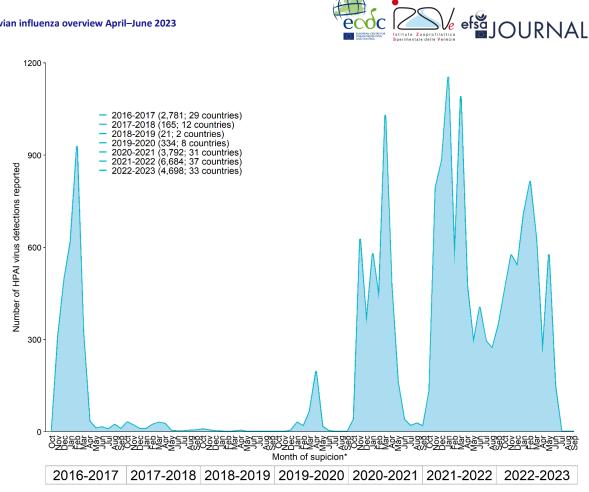
2.1.1 HPAI virus detections in birds in Europe

Figure 1 shows all HPAI outbreaks in birds that were reported via the Animal Disease Information System (ADIS) or the World Animal Health Information System (WOAH-WAHIS) in Europe for the last six and the current epidemiological years3 by month of suspicion. For the current epidemiological year 2022–2023, starting on 1 October 2022, data reported are truncated on 23 June 2023.

¹ According to Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016, point (9), 'poultry' means birds that are reared or kept in captivity for: (a) the production of: (i) meat; (ii) eggs for consumption; (iii) other products; (b) restocking supplies of game birds; (c) the purpose of breeding of birds used for the types of production referred to in points (a) and (b).

² According to Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016, point (10), 'captive birds' means any birds other than poultry that are kept in captivity for any reason other than those referred to in point (9), including those that are kept for shows, races, exhibitions, competitions, breeding or selling.

³ In this document an 'epidemiological year' refers to the period starting in week 40 (the beginning of October) and ending in week 39 (the end of September) of the following year, based on the dates on which the first HPAI virus detections were observed in wild birds in Europe in 2016–2017, 2020–2021 and 2021–2022.



^{*}If the date of suspicion was not available, the date of confirmation was used to assign the week of suspicion. United Kingdom data are from the Animal Disease Notification System (ADNS, former ADIS) up to 31 December 2020. From 1 January 2021 onwards, the data source was WOAH for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)⁴. Source: ADNS/ADIS and WOAH (data extraction carried out on 23 June 2023).

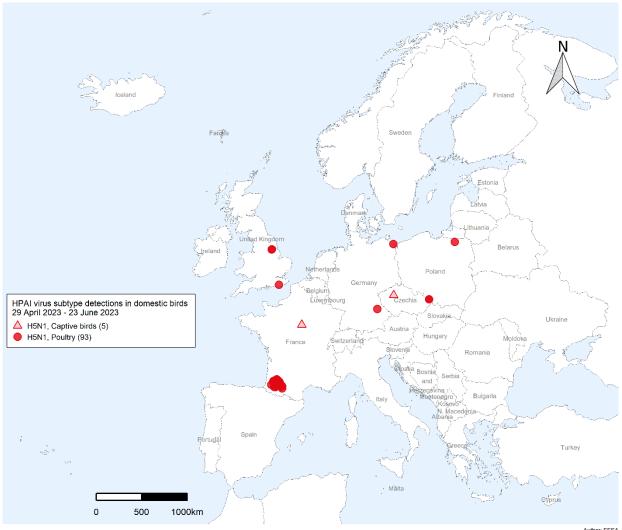
Figure 1: Distribution of the number of HPAI virus detections in domestic and wild birds reported in Europe during seven epidemiological years by month of suspicion, from 1 October 2016 to 23 June 2023 (18,475)

The HPAI epidemic observed in the 2021–2022 epidemiological year was the largest observed in Europe so far, with a total of 6,684 HPAI virus detections in 37 European countries, 2,761 of which in domestic birds and 3,923 in wild birds. In the current 2022-2023 epidemiological year, and as of 23 June 2023, a total of 4,698 HPAI virus detections were reported in 33 countries: 1,274 in domestic birds and 3,424 in wild birds (Figure 1, Table A.1 in Annex A). Considering the current reporting period, from 29 April to 23 June 2023, 732 HPAI virus detections were reported in poultry (93), captive (5) and wild birds (634) (Figure 2, Table A.1 in Annex A).

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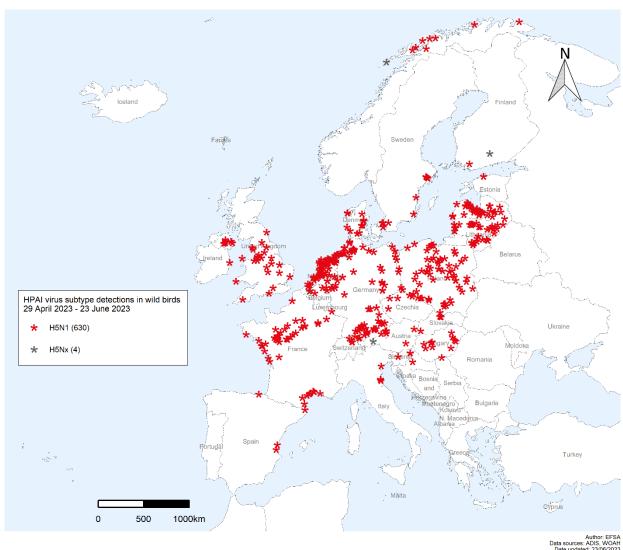
⁴ In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).





Author: EFSA Data sources: ADIS, WOAH Date updated: 23/06/2023





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*This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence. United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was WOAH for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)5.

Source: EFSA, ADIS and WOAH (data extraction carried out on 23 June 2023).

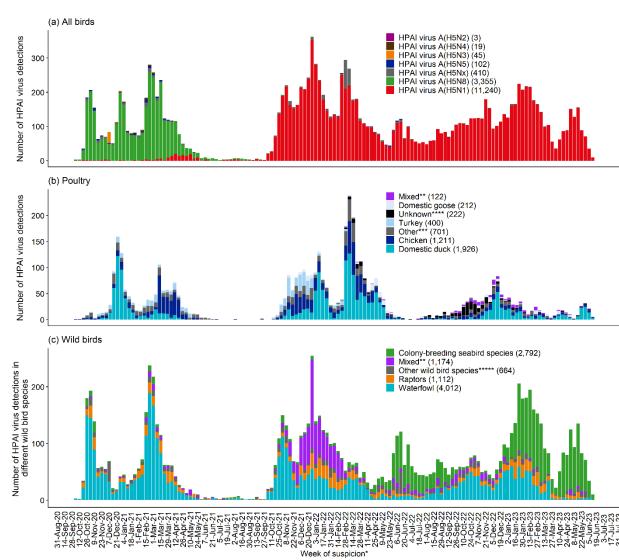
Figure 2: Geographic distribution, based on available geocoordinates, of HPAI virus detections in poultry and captive birds (98) (upper panel), and in wild birds (634) (lower panel) reported by virus subtype in Europe from 29 April to 23 June 2023

After a short decline in outbreaks reported in April, numbers appeared to be on the rise again in May. This temporal behaviour in the number of cases between May and June is similar to the behaviour observed during the 2021–2022 epidemic year in wild birds and is possibly linked to the fact that, in April, highly-susceptible wild bird chicks had not yet

⁵ In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).



hatched, whereas they are now fledging and spreading HPAI viruses in breeding colonies during the summer (Figure 3).



United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was WOAH for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)⁶.

Source: ADNS/ADIS, EFSA and WOAH (data extraction carried out on 23 June 2023).

*If the date of suspicion was not available, the date of confirmation was used to assign the week of suspicion.

- **'Mixed' refers to outbreaks in which multiple species or categories were involved.
- ***'Other' groups all other affected categories that are not indicated in the legend.

**** Unknown' refers to affected categories that were not further specified during reporting.

***** 'Other wild bird species' groups all other affected categories that are not indicated in the legend.

Figure 3: Distribution of the total number of HPAI virus detections reported in Europe by week of suspicion (dates indicate the first day of the week) and virus subtype (15,174) (a), affected poultry categories (4,794) (b) and affected wild bird categories (9,754) (c), from October 2020 to 23 June 2023

Most of the outbreaks in poultry were concentrated in Southwest France, whereas outbreaks in wild birds were widely reported from large parts of Europe, from the northernmost parts of Norway down to the Mediterranean coast. As observed during summer

⁶ In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).



last year, the surge of outbreaks in seabirds did not match the increase in the number of poultry outbreaks, neither geographically nor temporally (Figure 3). This is different from what was observed during the winter, when HPAI viruses mainly circulated in waterfowl.

Spatio-temporal information on all HPAI virus detections that have been reported in Europe since October 2016 is available via EFSA's interactive dashboard⁷.

Domestic birds

HPAI outbreaks in poultry were all identified as HPAI A(H5N1) and reported in France (85), the United Kingdom (3), Czechia (2), Germany (2) and Poland (1) (Figure 4). Overall, almost 980,000 birds died or were culled in the HPAI-affected poultry establishments with France accounting for 66% of the birds that died or were culled (corresponding to 91% of the affected establishments), followed by the United Kingdom with 19% and Germany with 7% (Figure 4).

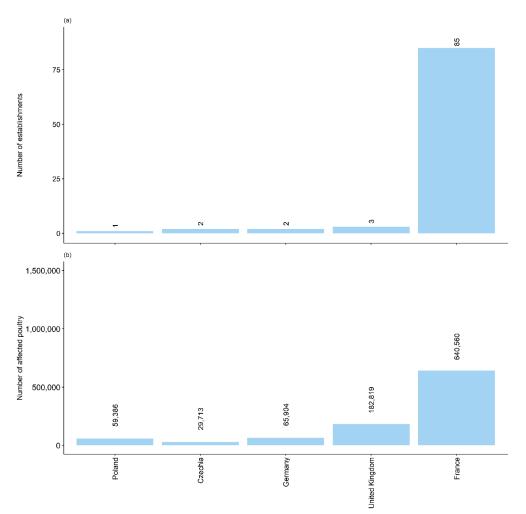


Figure 4: Number of HPAI virus-affected establishments (93) (a) and number of poultry in the HPAI virus-affected establishments (978,382) (b) in Europe between 28 April and 23 June 2023

During the current reporting period, particularly after a short decline in April, an increase in the number of outbreaks in poultry has been observed, driven by a local epidemic in

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⁷ http://hpai.efsa.aus.vet/



domestic ducks in Southwest France (Figure 2). This epidemic does not seem to overlap with outbreaks in wild birds, neither geographically nor phylogenetically: HPAI viruses sequenced so far from these poultry outbreaks all belonged to a single genotype and were directly related to HPAI viruses previously identified in December 2022–January 2023 from poultry outbreaks in the same area. On the other hand, sequenced HPAI viruses from wild birds in France during this reporting period belonged to a different genotype. This discrepancy suggests that the observed epidemic may have mainly been driven by extensive secondary spread within the affected poultry population, following increased density and an increase in poultry movements after restocking events had taken place. A similar cluster of outbreaks in a similar production system, i.e. due to secondary spread in a high poultry density area, was observed during the previous reporting period in Hungary.

In the following, a brief description of HPAI outbreaks in poultry is given by country. Information on the HPAI-affected establishments here reported was collected from the affected countries up to outbreaks that occurred by 9 June 2023.

Details on the characteristics of the affected poultry establishments and species reared are presented in <u>Annex C</u>, which also reports information on poultry outbreaks that occurred before the current reporting period and were therefore not included in the previous Scientific Report (EFSA et al., 2023) (i.e. from 2 March to 28 April 2023).

Czechia

During this reporting period, one primary and one secondary poultry outbreaks were reported in Czechia. Both occurred in commercial farms keeping turkeys for fattening, where birds did not have any outdoor access. For the primary outbreak, the most likely source of introduction was indirect contact with wild birds, as HPAI virus-positive wild birds were found at waterbodies around the farm. For the secondary outbreak, the most likely source of introduction was indirect contact with poultry, due to the close proximity to the other affected farm. Increased mortality among turkeys was reported for the primary outbreak, whereas a drop in food and water intake as well as other clinical signs were characteristic for both outbreaks. A total of 30 people were reported as exposed on both farms combined.

France

The majority of the 85 poultry outbreaks reported in France during this reporting period were secondary and all outbreaks occurred in commercial farms. Most of the farms (83) kept only one species of poultry, whereas two farms kept two species of poultry. The species reared on the mono-species farms were mulard ducks (hybrid between domestic Muscovy ducks and domestic ducks) for foie gras production (66), chickens for egg production (5), fattening (5) and breeding (1), domestic ducks for breeding (3) and other production (2), and domestic geese for fattening (1). The two multi-species farms both kept mulard ducks for foie gras production and chickens for fattening. For the 24 farms for which information on outdoor access was available, 19 reported that poultry did not have outdoor access and five farms reported that birds had outdoor access. No information on the most likely source of introduction was available at the time of publication of this report. Increased mortality was reported in 24 of the farms keeping ducks, for three of the farms this information was not available. Information on unspecified clinical signs was available for all farms keeping ducks and reported in 36 farms. Information on drop in feed and water intake was available for eight farms, all of which reported a drop. Drop in egg production was reported for one of the breeding duck farms, but this information was not provided for the two other farms. For



chickens, information on mortality and presence of unspecified clinical signs was available for all farms. Four of the farms reported increased mortality and 11 reported presence of unspecified clinical signs. The one farm keeping domestic geese for fattening reported no increased mortality but presence of unspecified clinical signs. No data on the number of exposed people was available at the time of publication of this report.

Germany

Two primary outbreaks were reported in Germany in May. Both outbreaks occurred in commercial farms keeping chickens, one for breeding and one for egg production. The birds did not have outdoor access and the most likely source of introduction was unknown. Both farms reported increased mortality and presence of unspecified clinical signs. It is unknown whether there was a drop in feed and water intake or egg production. No data on the number of exposed people was available at the time of publication of this report.

Poland

One primary poultry outbreak was reported in the region Warmińsko-Mazurskie at the end of May. The establishment was a commercial farm keeping turkeys for fattening. The birds did not have outdoor access and the most likely source of introduction was indirect contact with wild birds due to the proximity of the farm to wild bird habitat. Increased mortality, a drop in feed and water intake and the presence of other clinical signs were reported on the farm. The number of exposed people was eight.

Control and prevention measures applied in the affected Member States following HPAI outbreaks that occurred up to 9 June 2023 in poultry are described in <u>Annex B</u>, thanks to the countries that were willing to collaborate with EFSA and kindly provided the information reported.

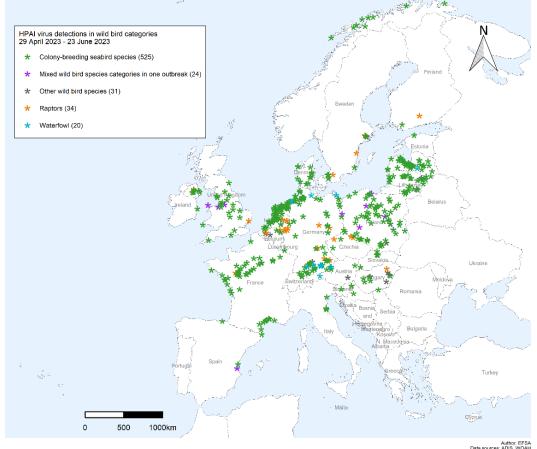
HPAI virus detections in captive birds, all due to A(H5N1) viruses, were reported in Czechia (1) and France (4) (Figure 2, Table A.1 in <u>Annex A</u>). In France, 4 A(H5N1) virus detections were reported in domestic ducks (1), mixed species including domestic waterfowl (2, including in domestic chickens in 1) and domestic chickens (1).

Wild birds

In contrast to the low number of HPAI outbreaks in poultry (except for France), there was a high number of HPAI virus detections in wild birds: 630 A(H5N1) and four A(H5Nx) virus detections were reported in Germany (221), Poland (71), the Netherlands (68), Latvia (49), France (47), Lithuania (37), the United Kingdom (32), Denmark (18), Austria (15), Hungary (13), and Belgium, Croatia, Czechia, Estonia, Finland, Ireland, Italy, Luxembourg, Norway, Serbia, Slovakia, Slovenia, Spain, Sweden and Switzerland (1 to 9 each) (Figure 2, Table A.1 in <u>Annex A</u>). The overall number of HPAI virus detections (634) was slightly lower than the one of the previous reporting period (723 from 2 March to 28 April). However, the number of seabirds identified to species was higher than the one of the previous reporting period (438 vs 351). This was due to the higher number of reported HPAI virus detections in the current compared to the previous reporting period for common terns (48 vs 2), European herring gulls (32 vs 15) and brown-headed gulls (13 vs 4), and because HPAI viruses were detected in several tern (sandwich, arctic, royal) and gull species (Mediterranean, mew, arctic herring, grey-headed, slender-billed) as well as black-legged kittiwakes in the current but not in the previous reporting period.



The geographic distribution of reported HPAI virus detections in wild birds was widespread, from north (north coast of Norway) to south (east-central Spain), and from east (Latvia) to west (Ireland) (Figure 2, Figure 5). Foci of reported HPAI virus detections were centred in the Wadden Sea region (Netherlands, Germany, Denmark) and Northeast Europe. These foci consisted mainly of colonial seabirds, co-localised with smaller numbers of raptors and waterfowl (e.g. around Lake Constance). The geographic distribution was similar to the one of the previous reporting period, except for reported detections on the north coast of Norway, in the Baltic states, and in the western part of the Mediterranean Sea, along the French coastline (Figure 5). Compared to the situation observed in 2022, seabird species were not only found dead along coastlines but also inland (Figure A.1 in Annex A), which may be explained by the shift in the proportions of seabird species affected and their respective breeding grounds. The complete list of wild bird species found as HPAI virus-infected from 29 April to 23 June 2023 is reported in Figure A.2 in Annex A.



Date updated: 23/06/2023

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*This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice Opinion on the Kosovo Declaration of Independence. Note that the unit reported is the number of HPAI virus detections in different wild bird species and not the number of HPAI virus detections in wild birds (as more than one species can be involved in one single HPAI virus detection reported).

Source: ADIS, EFSA and WOAH (data extraction carried out on 23 June 2023).

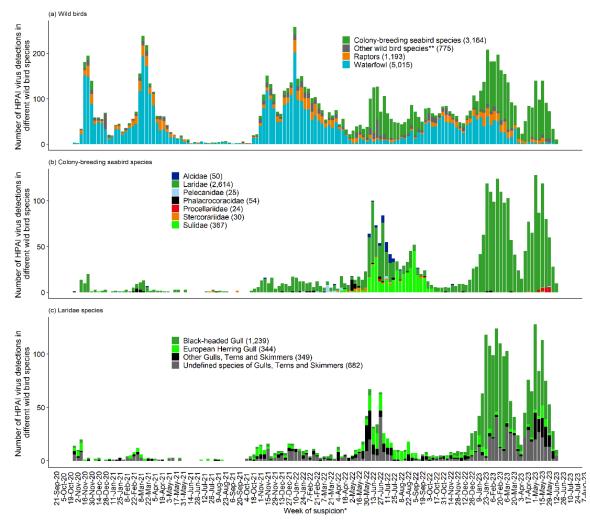
Figure 5: Geographic distribution, based on available geocoordinates, of HPAI virus detections in different categories of wild birds in Europe, by species category, from 28 April to 23 June 2023



Following a decline in reported HPAI virus detections in wild birds at the beginning of April, there was an increase in the current reporting period (29 April to 23 June) with a peak in the month of May (Figure 3).

As observed during the previous two reporting periods, the vast majority of wild birds reported as HPAI virus-infected were colony-breeding seabirds (525 of 634) (Figures 3, Figure 5), particularly gulls and terns (family Laridae, 438), and, to a lesser extent, Procellariidae (18) (Figure A.2 in Annex A, Figure 6). Compared to the previous reporting period, less HPAI virus detections were reported in waterbirds (20 vs 107) and raptors (34 vs 86), but more in colony-breeding seabirds (525 vs 499) and the mixed wild bird species category (25 vs 9). Of the gulls and terns identified to species, nearly all were black-headed gulls (312), with a smaller number of common terns (48) and European herring gulls (32) (Figure 6, Figure A.2 in Annex A). Regarding waterfowl (20) (Figure 5), most of the HPAI virus detections were reported in mallards (7). Regarding raptors (34) (Figure 5), HPAI virus detections were most frequently reported in peregrine falcons (12). The number of HPAIaffected wild birds that were not identified to species was 180/669 (27%), a substantial improvement compared to the previous reporting period (260/732, 36%) (Figure A.2 in Annex A). Note that Figures 5 and 6 as well as Figure A.2 in Annex A provide information on the numbers of wild bird categories/families/species that have been detected as affected within the HPAI virus detections reported in wild birds and that more than one bird category/family/species can be involved in one single HPAI detection reported.





*If the date of suspicion was not available, the date of confirmation was used to assign the week of suspicion. **Other wild bird species' contain unknown species or categories different from those displayed. The complete list of species by each wild bird category is reported in Table A.3 in <u>Annex A</u>.

Note that the scale of the vertical axes is specific to each panel and that the unit reported is the number of HPAI virus detections in different wild bird species and not the number of HPAI virus detections in wild birds (as more than one species can be involved in one single HPAI virus detection reported).

United Kingdom data are from ADNS up to 31 December 2020. From 1 January 2021 onwards, the data source was WOAH for the United Kingdom (excluding Northern Ireland) and ADNS/ADIS for the United Kingdom (Northern Ireland)⁸.

Source: ADNS/ADIS, WOAH (data extraction carried out on 23 June 2023) and EFSA.

Figure 6: Distribution of the total number of HPAI virus detections reported in Europe by week of suspicion (dates indicate the first day of the week) and (a) affected wild bird categories (10,147), (b) affected colony-breeding seabird families (3,164), and (c) affected Laridae species (2,614), from October 2020 to 23 June 2023

Of note, HPAI virus detections in wild birds are generally underestimated and the numbers provided are not representative of the number of wild birds that actually died from A(H5) infection.

The increase in reported HPAI virus detections in wild birds from April to May and June in the current reporting period corresponds to an increase in reported mass mortality events in hatched juvenile seabirds. While seabird mortality in the previous reporting period

⁸ In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data sampling are also applicable to the United Kingdom (Northern Ireland).



involved adult seabirds, mainly black-headed gulls, in the current reporting period, since the beginning of June, mortality also involved juvenile birds. Reports of hundreds to thousands of HPAI virus-associated deaths per breeding colony were reported in adult and/or juvenile black-headed gulls in the Netherlands (Sovon, online), Belgium (Natuurpunt, online-b), the United Kingdom (BTO, online) and Sweden (SVA, online-c). Besides black-headed gulls, HPAI virus-associated mortality was also recorded in seabird colony sites of other species during this reporting period: 40% of 800 common terns at one breeding colony and 50% of 400 common terns at another breeding colony in North Wales were reported dead from HPAI during this reporting period (BTO, online); 515 sandwich terns, 23 gull-billed terns and 2 common terns were reported dead from HPAI in a mixed-species breeding colony in Albufera, Valencia, Spain (IM Veterinaria, online); more than 4000 birds, of which 86% black-headed gulls and 14% common terns, were reported dead from HPAI from a mixed-species breeding colony on Stern Island, River Eems, the Netherlands (Nature Today, online); 1,200 juvenile birds, of which 750 black-headed gulls, 240 sandwich terns, and 130 Mediterranean gulls were reported dead from HPAI at breeding colonies in the Haringvliet, the Netherlands (Deltamilieu Projecten, online); more than 1,400 juveniles were reported dead from HPAI and there was increased mortality in adults at a sandwich tern breeding colony in Zeebrugge, Belgium (Volgelbescherming, online-a); more than 30 black-legged kittiwakes were reported dead from HPAI in Leirvag, Harstad, Norway (nrk, online). Besides in seabirds, it was estimated that there was a 15% decrease in successful breeding pairs of peregrine falcons in Belgium due to HPAI virus-associated deaths in adult birds in February and March of 2023 (Natuurpunt, online-a). Another mass mortality event with 1,460 dead chicks involved was reported at the end of June in a colony of sandwich terns breeding in the Veneto region, Italy (EURL communication). Besides in sandwich terns, A(H5N1) outbreaks were also reported in yellow-legged gulls, slender-billed gulls and Mediterranean gulls in Italy.

The effect of HPAI in 2022 was reported to have substantial effects on wild birds at the population level. In Belgium, it was estimated that one-third of the black-headed gull population had died from HPAI (Nieuwsblad, online). In the Netherlands and Flanders, the number of breeding pairs of sandwich terns in 2023 was less than half of the one in 2022 (9,000 vs 19,000) and breeding colonies that were severely affected in 2022 stayed vacant in 2023 (Volgelbescherming, online-b). Since the sandwich tern is a long-lived species that raises an average of one chick per breeding pair, it is expected to take many years until the population recovers from the HPAI mortality in 2022, let alone ongoing mortality in 2023. In the United Kingdom, declines of breeding success on the islands Lewis and Harris from 55% in 2021 to 16% in 2022 in golden eagles and from 66% in 2021 to 24% in 2022 in white-tailed eagles were attributed to HPAI based on studies by the British Trust of Ornithology (BTO), using data from the Scottish Raptor Monitoring Scheme (BBC, online).

2.1.2 HPAI virus detections in birds outside Europe

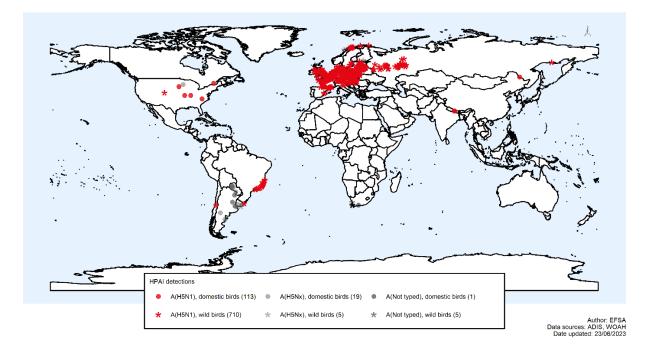
An overview of the HPAI virus detections in birds that were notified from other countries not reporting via ADIS but via WOAH from 29 April to 23 June 2023 is presented in Table 1 and Figure 7.



Table 1: Number of HPAI virus detections in non-European countries, by virus subtypeand country, from 29 April to 23 June 2023

	Country	Domestic birds		Wild birds				
Region		A(H5N1)	A(H5Nx)	A (Not typed)	A(H5N1)	A(H5Nx)	A (Not typed)	Total
Africa (6)	South Africa	-	-	1	-	-	5	6
	Argentina	-	10	-	-	-	-	10
	Brazil	-	-	-	41	-	-	41
	Canada	1	-	-	-	-	-	1
Americas	Chile	1	-	-	-	-	-	1
(68)	Paraguay	-	5	-	-	-	-	5
	United States							
	of America	4	1	-	1	-	-	6
	Uruguay	-	3	-	-	1	-	4
Asia (5)	Nepal	5	-	-	-	-	-	5
Europe (42)	Russia	4	-	-	38	-	-	42
Total		15	19	1	80	1	5	121

'-' means that no HPAI outbreaks were notified to WOAH. Source: WOAH (data extraction carried out on 23 June 2023).



Disclaimer: The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the European Food Safety Authority concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Figure 7: Geographic distribution, based on available geocoordinates, of HPAI virus detections reported in domestic birds (133) and wild birds (720) by virus type, from 29 April to 23 June 2023

Compared to the previous reporting period, fewer HPAI outbreaks in poultry but more HPAI virus detections in wild birds were reported to WOAH overall. Furthermore, the number of countries submitting data to WOAH has decreased considerably. Specifically, from the regions of Africa and Asia, only South Africa and Nepal, respectively, reported HPAI



outbreaks in domestic poultry and wild birds during the current reporting period. In the Americas, the number of affected countries has remained stable, but in contrast to the last report, Bolivia, Colombia and Panama did not report any further A(H5) virus detections. Brazil and Paraguay, not previously affected, reported for the first time A(H5) virus detections during this reporting period.

South Africa reported an outbreak of A(H5) in a very large poultry farm in the Western Cape province and detected A(H5) virus in greater crested terns, common terns and kelp gulls. Furthermore, South Africa notified two A(H7) outbreaks in large commercial poultry farms in the northeast of the country (Flu Trackers, online). Although occurred during the previous reporting period and due to late reporting, A(H5) was reported in 752 wild birds, of which 740 died, on Iles Kapatchez, Guinea, West Africa (WOAH, online-a). It involved unspecified terns and pelicans. Nepal notified several A(H5N1) virus detections in small- to medium-sized poultry establishments from the same region, near the border to India, which had been affected before. In Russia, A(H5N1) virus was detected in two backyard flocks and two very large poultry farms as well as in many wild birds of the family Laridae and Alcidae (unspecified), mainly in the western part of Russia. Compared to the last report, the number of A(H5) outbreaks in poultry farms in Canada and the United States of America has decreased to one-tenth of the outbreaks in the previous reporting period. The United States of America reported wild bird cases of A(H5N6), clade 2.3.4.4b (reassortant with an American lineage N6 segment), in a bald eagle to WOAH. Furthermore, outside the present reporting period, A(H5N5), fully Eurasian lineage clade 2.3.4.4b, was detected in February and March 2023 in great black-backed gulls. No A(H5) outbreaks were reported to WOAH from Central America, while in South America the HPAI epidemic in domestic poultry continued at a lower level. Paraguay has notified its initial occurrence of five A(H5) outbreaks in backyard poultry farms in the north-western region of Chaco (ProMed, online-a; UH 50, online). In addition to ferruginous hawk in the United States of America and greylag goose as well as turkey vulture in Uruguay, A(H5N1) virus has been detected in several wild bird species on the Brazilian Atlantic coast as, e.g. black-necked swan, royal tern, common tern, South American tern, Cabot's tern, grey-headed gull, brown booby, magnificent frigatebird, neotropic cormorant, great black hawk, roadside hawk and tropical screech owl. The actual situation in the Americas is continuously evolving with new HPAI virus detections in wild and domestic birds as well as in mammal species.

The list of wild bird species that have been reported to WOAH as HPAI virus-infected from 29 April to 23 June 2023 is presented in Table A.2 in <u>Annex A</u>.

HPAI A(H5) virus detections in poultry, mammals and wild birds are also reported to the public via different means, e.g. this is the case for the following outbreaks than those displayed in Table 1. However, in the tables and figures of the current report, only the data extracted from WOAH on 23 June 2023 are presented; information available from other sources has not been systematically retrieved and is only described in the text. This additional information about HPAI virus detections, not reported in WOAH-WAHIS, is reported below.

The Agência Brasil reported the confirmation of the first case of HPAI A(H5) in a small poultry farm with mixed species in the state of Espírito Santo by the Ministry of Agriculture of Brazil. Furthermore, 50 cases of A(H5N1) have been detected in wild birds in seven Brazilian states, including Espírito Santo (Agencia Brasil, online; ib, online; Pregon, online). The Servicio Agrícola y Ganadero (SAG) of the Chilean Ministry of Agriculture reported large mortality events in various wild bird species due to A(H5) since December 2022 (SAG,



online). In the current reporting period, Argentina informed the public about outbreaks in backyard and poultry farms as well as wild birds in different regions of the country (Senasa, online). In Peru, Servicio Nacional de Sanidad Agraria del Perú also confirmed the continuous presence of HPAI in backyard poultry (ILO Noticias, online). Nigeria reported to FAO's EMPRES-i an outbreak of HPAI A(H5N1) on a medium-sized farm in a previously affected area (FAO, online-a).

2.1.3 Genetic characteristics of HPAI viruses of the A(H5N1) subtype circulating in Europe in avian species

Details on the nomenclature of the HPAI A(H5) viruses used in this section are reported in Appendix B.

Genetic diversity of HPAI A(H5N1) viruses in avian species

Six main genotypes corresponding to more than 98% of the HPAI A(H5N1) characterised viruses (> 1300) from 22 European countries have been identified since October 2022. Four of these genotypes have been circulating in Europe since the 2021–2022 epidemiological year, while the others have newly emerged, very likely from reassortment events with avian influenza viruses circulating in Eurasian wild bird populations. Between October 2022 and January 2023, the majority of the characterised viruses belonged to the AB genotype (H5N1-A/duck/Saratov/29-02/2021-like). However, a rapid increase in the number of detections of the BB genotype (H5N1-A/Herring_gull/France/22P015977/2022-like) was observed starting from December 2022. Since February 2023, the BB genotype has become the most frequently identified variant, reaching in April–May 2023 a frequency of about 90%, based on the data available.

The vast majority of genotype BB viruses have been identified in gulls, with the blackheaded gull representing the most affected species during the ongoing epidemic. This genotype has showed a recent wide geographic expansion. During the past winter season it mainly circulated in Western Europe (Austria, Belgium, France, Germany, Italy, Netherlands, Spain, Switzerland, United Kingdom), whereas since spring 2023, it has spread eastward, reaching for the first time Croatia, Czechia, Denmark, Luxembourg, Norway, Poland and Sweden, where mass mortality events in Laridae were reported. Genetic clustering indicates the occurrence of multiple virus introductions of this genotype in the affected countries. Moreover, genetic data indicates that viruses of the BB genotype identified in sandwich terns and gulls along the Mediterranean coasts (Italy and France) are closely related to viruses recently identified in wild birds in Africa, which is possibly due to a new virus incursion in Europe that took place during the spring migration.

In domestic birds, AB and CH (H5N1-A/Mallard/Netherlands/18/2022-like) have been the most frequently detected genotypes during the 2022–2023 epidemiological year. However, starting from February 2023, the number of poultry outbreaks associated to the BB genotype has increased. The A(H5N1) viruses that caused multiple outbreaks in Southwest France during this reporting period belong to genotype CC (H5N1-A/chicken/Germany-NI/AI04794/2022-like), which had been identified in poultry farms in the same geographic area between December 2022 and January 2023.

Mutations identified in HPAI A(H5N1) viruses from avian species

Molecular analyses of the A(H5N1) viruses circulating in birds in Europe during the 2022– 2023 epidemiological year indicate that they continue to be well-adapted to avian species,

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as they retain a preferential binding for avian-like receptors. However, several mutations, previously described in literature (Suttie et al., 2019), have been identified as being associated with i) enhanced polymerase activity and replication in mammals or mammalian cells, ii) increased virulence, iii) increased/conferred resistance towards antiviral drugs, iv) increased in vitro binding to human-type receptors alpha2,6-SA, v) decreased antiviral response in ferrets, vi) evasion of human butyrophilin subfamily 3 member A3 (BTN3A3), and vii) disruption of the second SIA-binding site, with a frequency varying for the distinct mutations. The real effect of these mutations on the biological characteristics of the viruses is still unknown and further studies are needed to improve existing knowledge. Among the identified mutations, molecular markers associated with an increased replication and/or virulence in mammals were rarely detected in birds, as observed in the previous epidemiological years. Specifically, since October 2022, mutations PB2-E627K, PB2-D701N and PB2-T271A have been observed in five viruses collected from wild (2 PB2-627K) and domestic (1 PB2-E627K, 1 PB2-D701N, 1 PB2-T271A) birds in different European countries. Among the mutations in the HA protein which have proved to increase in vitro binding to human-type receptor, some of them (i.e. S133A, S154N, T156A, H5 numbering) have been identified in the majority of the A(H5N1) viruses circulating in Europe since October 2022, while others (i.e. D94N, S155N, T188I, Q192R, V210I) have only been sporadically observed. The impact of these HA mutations on the biological characteristics of the circulating viruses is still unknown; however, none of them have been demonstrated to cause a shift from avian-like to human-like receptor binding preference. Mutations associated with antiviral resistance have only been occasionally identified in the circulating viruses. Moreover, almost all the A(H5N1) viruses belonging to the BB genotype (H5N1 A/gull/France/22P015977/2022-like) contain mutations NP-Y52N (Pinto et al., 2023) and NA-S369I (Du et al., 2018), which may increase their zoonotic potential.

2.2 HPAI virus detections in non-human mammals

2.2.1 HPAI virus detections in non-human mammals worldwide

In wild mammals, HPAI A(H5N1) virus detections during this reporting period were reported in red fox (Vulpes vulpes), skunk (Mephitis mephitis), American black bear (Ursus americanus) and raccoon (Procyon lotor) in the United States of America. A(H5N1) virus was also identified from a captive caracal (Caracal caracal) (first time) in Łódzkie, Poland. Moreover, at the beginning of April 2023 (before this reporting period), A(H5N5) virus was detected in a raccoon in Canada (WOAH, online-d). Unknown and A(H5Nx) virus detections occurred in red fox in Belgium and Sweden, as well as South American sea lion (Otaria *flavescens*) and Southern river otter (*Lontra provocax*) (first time) in Chile. Twenty-three South American coatis (Nasua nasua) were found infected with A(H5Nx) virus in Uruguay after four cases had been detected in a zoo in Germany last year (Table 2). Mortality in at least 80 South American sea lions (Otaria flavescens) due to avian influenza was suspected on the coastline of Peru (Prensa regional, online) and A(H5) was also reported by the Chilean government in a South American sea lion found dead in Puerto Williams, Chile, on 14 June 2023, at the southernmost tip of the American continent (Polar Comunicaciones, online). All other HPAI virus detections in mammals that occurred before 29 April, but were only reported during the current reporting period, are included in Table 2.

During this reporting period, A(H5N1) virus infections were also reported in domestic mammals: in a domesticated cat (*Felis catus*) and five dogs (*Canis lupus familiaris*) in Italy, where seroconversion in asymptomatic animals was reported, and in cats in Poland (Dr Krzysztof Jażdżewski, 2023; Glowny Inspektorat Weterynarii, online-f, d, c, b) (Table 2).



In Poland, as of 10 July 2023, 24 domestic cats, out of 46 tested, have been identified as A(H5N1) virus-infected, with the first case with clinical signs reported on 10 June 2023. As of 11 July 2023, one more sample is currently being analysed. Sampled cats were between seven months and eight years of age, and came from eight voivodeships (6 from Lubelskie, 6 from Pomorskie, 3 from Mazowieckie, 2 from Dolnośląskie, 2 from Kujawsko-Pomorskie, 2 from Opolskie, 2 from Warmińsko-Mazurskie, 1 from Wielkopolskie), including the surroundings of major cities such as Bydgoszcz, Gdańsk, Gdynia, Krákow, Lublin, Poznań, Pruszcz Gdański, Tri-city metropolitan area and Wrocław. Geographical locations of the cases reported are widely spread across the country and do not suggest feline-to-feline transmission. Disease development in affected cats has been described as acute with the most frequent clinical signs being of respiratory (e.g. dyspnoea) and neurological nature (e.g. paralysis, epilepsy, nystagmus). While some cats survived A(H5N1) virus infection, several cats died (on average five days after onset of clinical signs, the last one on 30 June 2023), of which nine were euthanised. It remains unclear as to how many cats have been showing clinical signs since the first case was reported on 10 June 2023, as not all cats are accessible for sampling and laboratory testing. At the time of writing this report, 17 epidemiological investigations are ongoing to determine the source of infection, including interviews with veterinarians and cat owners, which to this date remains unknown. Among the affected cats, 13 were kept indoors with only occasional access to outdoor areas (i.e. balconies or terraces), whereas four were free-ranging and reportedly had contact with wildfowl. Raw poultry meat and offal were fed to 13 of the affected cats, but the exact time of feeding is unknown and no causal relationship has been established. Official tests on feed samples consumed by infected cats and tracing back of feed have not been performed so far. Due to the occurrence of HPAI in an animal species for which no administrative eradication action is being taken, for the time being Polish authorities are focusing on the coordination of the sampling of animals, testing of samples sent by private and official veterinarians in the national reference laboratory, carrying out the epidemiological investigation and collaboration with the Medical Service to monitor people having contact with sick animals. Recommendations from the Polish veterinary authorities can be found at the statements from the Chief Veterinary officer (Dr Krzysztof Jażdżewski, 2023; Glowny Inspektorat Weterynarii, online-e, a, f, d, c, b) and the Chief Sanitary Inspectorate (Glowny Inspektorat Sanitarny, online).

With regard to the Italian cases, on 22 May 2023, the EURL confirmed the serological positivity of five asymptomatic dogs and one cat against A(H5N1) by haemagglutinin inhibition, microneutralization and enzyme-linked immunosorbent assay. The mammals came from a backyard poultry farm in which in April an outbreak of A(H5N1), clade 2.3.4.4b, genotype BB, had been notified. The virus collected from poultry had a mutation considered a marker of adaptation of viruses to mammals (T271A in the PB2 protein), which may increase its zoonotic potential.

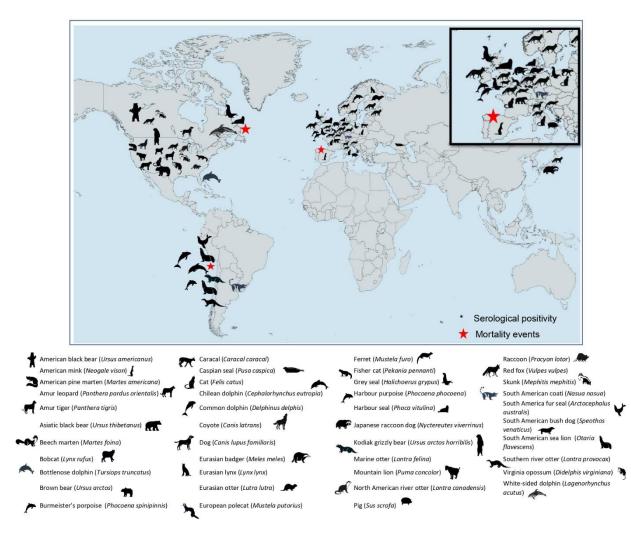
Earlier this year, in January 2023, another cat had been found infected with A(H5N1) virus in Canada (WOAH, online-d).

Molecular and serological screening of over 500 dead wild carnivores was performed in the Netherlands for A(H5) virus infection. There was virological evidence for A(H5) virus infection in 0.8%, 1.4% and 9.9% of animals tested in 2020, 2021 and 2022, respectively, with the highest proportions of positives in foxes (9/31, 29%), polecats (4/17, 24%) and stone martens (6/400, 2%). Infections were also found in animals without associated neurological signs or mortality. Serological evidence of infection was detected in 20% of the



study population, including foxes (7/19, 37%), polecats (2/2, 100%) and stone martens (71/126, 56%). These findings suggest that a substantial number of wild carnivores are infected but undetected by current surveillance programs (Irina et al., 2023).

The geographic distribution of A(H5) viruses, clade 2.3.4.4b, that have been reported in non-human mammals since 2016 is presented in Figure 8.



Disclaimer: The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the European Food Safety Authority concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The square in the top right corner of the map highlights the situation in North Europe.

Figure 8: Geographic distribution of HPAI virus detections in non-human mammals since 2016 (based on Table 2)

The wild mammal species involved are mainly those that hunt wild birds, feed on dead wild birds, or both. The species in which A(H5N1) virus was most frequently reported is the red fox, which occurs all across Europe, North Africa, most of Asia (apart from the extreme Southeast), and North America (except Southwest USA and Mexico) (GBIF, online; IUCN, online). The frequent detection of A(H5N1) virus in red foxes is likely a consequence of its wide distribution, which largely overlaps with the geographic spread of the HPAI A(H5N1) outbreaks, and its diet, which partly includes both hunted and scavenged wild birds.



Virus	Animal (order, family, species)			Country	Reference	
0	Artiodactyla	Suidae	Domestic pig (<i>Sus scrofa</i>)*	France	(Herve et al., 2021)	
p			Wild boar (Sus scrofa)*	Germany	(Schülein et al., 2021)	
clade 4b	Carnivora	Canidae	Red fox (Vulpes vulpes)	United Kingdom	(Floyd et al., 2021)	
:N8) 3.4.2		Phocidae	Grey seal (Halichoerus grypus)	Poland, Sweden, United Kingdom	(Shin et al., 2019; Floyd et al., 2021; SVA, online- b; personal communication by Siamak Zohari, SVA)	
A(H5N8) 2.3.4.4			Harbour seal (<i>Phoca vitulina</i>)	Denmark, Germany, United Kingdom	(Floyd et al., 2021; Ärzteblatt, online; Avian Flu Diary, online-b; Outbreak News, online; SSI, online a)	
	Artiodactyla	Suidae	Domestic pig (Sus scrofa)*	Italy	(Rosone et al., 2023)	
	Carnivora	Canidae	Common raccoon dog (<i>Nyctereutes</i> procyonoides)	Japan	(WOAH, online-c)	
			Coyote (Canis latrans)	United States of America	(WOAH, online-c)	
			Dog (Canis lupus familiaris)	Canada, Italy*	(WOAH, online-d, personal communication by EURL)	
A(H5Nx) clade 2.3.4.4b			Japanese raccoon dog (Nyctereutes viverrinus)	Japan	(FAO, online-b)	
			Red fox (Vulpes vulpes)	Belgium, Canada, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Japan, Netherlands, Norway, United Kingdom, United States of America, Sweden	(SVA, online-b; USDA, online; WOAH, online-b, c); personal communication by Siamak Zohari, SVA; Irish National Reference Laboratory for Avian Influenza, personal communication; SSI, online-b)	
			South American bush dog (Speothos venaticus venaticus)	United Kingdom	(WOAH, online-d)	
Ă		Felidae	Amur leopard (Panthera pardus)	United States of America	(USDA, online)	
P			Amur tiger (<i>Panthera tigris</i>)**	United States of America	(WOAH, online-c)	
с Г			Bobcat (Lynx rufus)	United States of America	(WOAH, online-c)	
A(H5N1)			Caracal (Caracal caracal)	Poland	(Personal communication by Dr Krzysztof Jażdżewski, CVO Poland)	
A(I			Cat (<i>Felis catus</i>)	Canada, France, Italy [*] , Poland, United States of America France, USA, Italy	(WOAH, online-c; Briand Fx Fau - Souchaud et al., 2023)	
			Lynx (Lynx lynx)	Finland	(FFA, online)	
			Mountain lion (Puma concolor)	United States of America	(WOAH, online-c)	
		Mephitidae	Striped skunk (Mephitis mephitis)	Canada, United States of America	(CTV News, online; USDA, online; WOAH, online-c,	

Table 2: Avian influenza A(H5Nx) virus detections in mammal species other than humans related to circulating viruses worldwide, 2016–2023



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Animal (order, family, species)		Country	Reference
	Mustelidae	American mink (Neovison vison)	Canada, Spain	(WOAH, online-b; Xunta de Galicia, online)
		Beech marten (Martes foina)	Netherlands	(GISAID, online)
		Eurasian otter (Lutra lutra)	Netherlands, Finland	(WUR, online)
		European badger (Meles meles)	Netherlands	(WUR, online)
		European polecat (Mustela putorius)	Belgium, Netherlands	(WUR, online)
		Ferret (Mustela furo)	Belgium, Slovenia	(WOAH, online-c)
		Fisher cat (Pekania pennanti)	United States of America	(WOAH, online-c)
		Marine otter (Lontra felina)	Chile	(ProMed, online-b; WOAH, online-d)
		Mountain lion (Puma concolor)	United States of America	(WOAH, online-c)
		North American River otter (Lontra canadensis)	United States of America	(WOAH, online-d)
		Southern river otter (Lontra provocax)	Chile	(WOAH, online-c)
	Otariidae	South American sea lion (Otaria flavescens)	Chile, Peru	(WOAH, online-d)
		South American fur seal (Arctocephalus australis)	Peru	(FAO, online-b)
	Phocidae	Grey seal (Halichoerus grypus)	Canada, Germany, Netherlands, Poland, United Kingdom, United States of America	(AMMI, 2022; WOAH, online-b; Monica et al.,
		Harbour seal (<i>Phoca vitulina</i>)	Canada, Denmark, Germany, United Kingdom, United States of America	(Agriland, online; WOAH, online-c)
		Caspian seal (Pusa caspica)	Russia	(FAO, online-b)
	Procyonidae	Raccoon (<i>Procyon lotor</i>)	Canada, United States of America	(WOAH, online-c)
		South American coati (Nasua nasua)	Germany, Uruguay	(WOAH, online-c)
		South American fur seal (Arctocephalus australis)	Peru	(FAO, online-b)
	Ursidae	American black bear (<i>Ursus</i> americanus)	Canada, United States of America	(Healthy Wildlife, online; KTOO, online; WOA online-c)
		Asiatic black bear (Ursus thibetanus)	France	(GISAID, online; WOAH, online-d)
		Brown bear (Ursus arctos)	United States of America	(Kiniradio, online; USDA, online)
		Kodiak grizzly bear (<i>Ursus arctos</i> horribilis)	United States of America	(FAO, online-b)
Cetacea	Delphinidae	Bottlenose dolphin (<i>Tursiops</i> truncatus)	Peru, United States of America	(UFHealth, online; WOAH, online-c)
		Chilean dolphin (Cephalorhynchus eutropia)	Chile	(Acuicultura, 2023; FAO, online-b)



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Virus	Animal (order, family, species)			Country	Reference	
			Common dolphin (Delphinus delphis)	Peru, United Kingdom	(Leguia et al., 2023; WOAH, online-d)	
			White-sided dolphin (<i>Lagenorhynchus acutus</i>)	Canada	(Avian Flu Diary, online-a)	
		Phocoenidae	Burmeister's porpoise (Phocoena spinipinnis)	Chile (FAO, online-b)	(FAO, online-b)	
			Harbour porpoise (<i>Phocoena phocoena</i>)	Sweden, United Kingdom	(SVA, online-a)	
			White-sided dolphin (<i>Lagenorhynchus acutus</i>)	Canada	(Avian Flu Diary, online-a)	
	Didelphimorphia	Didelphidae	Virginia opossum (<i>Didelphis virginiana</i>)	United States of America	(USDA, online; WOAH, online-c)	
A(H5N5) clade 2.3.4.4b	Carnivora	Procyonidae	Raccoon (Procyon lotor)	Canada	(WOAH, online-d)	



2.2.2 Genetic characteristics of HPAI viruses of the A(H5N1) subtype circulating in Europe in non-human mammals

Details on the nomenclature of the HPAI A(H5) viruses used in this section are reported in Appendix B.

Genetic diversity of HPAI A(H5N1) viruses in non-human mammals in Europe

Since October 2020, the complete genome sequences of HPAI A(H5) viruses of clade 2.3.4.4b collected from 14 distinct mammalian species (European badger (*Meles meles*), Asian black bear (*Ursus thibetanus*), bush dog (*Speothos venaticus*), domestic cat (*Felis catus*), South American coati (*Nasua nasua*), ferret (*Mustela furo*), red fox (*Vulpes vulpes*), Eurasian lynx (*lynx lynx*), American mink (*Neovison vison*), Eurasian otter (*Lutra lutra*), European polecat (*Mustela putorius*), harbour porpoise (*Phocoena phocoena*), harbour seal (*Phoca vitulina*) and beech marten (*Martes foina*)) in 15 European countries have been generated. The characterised viruses belong to 8 different A(H5N1) and A(H5N8) genotypes previously identified in birds. During the 2022–2023 epidemiological year, most of the mammalian infections are caused by the three most widespread genotypes in birds, namely BB (H5N1-A/gull/France/22P015977/2022-like), AB (H5N1-A/duck/Saratov/29-02/2021-like) and CH (H5N1-A/Eurasian_Wigeon/Netherlands/3/2022-like). Based on the available data, the vast majority of the cases detected in wild mammals, mainly red foxes, in Europe in the last months (February–May 2023) belong to genotype BB, the most frequently detected in wild birds since February 2023.

About half of the characterised viruses contain at least one of the adaptive markers associated with an increased virulence and replication in mammals in the PB2 protein (E627K, D701N or T271A) (Suttie et al., 2019). These mutations have rarely been identified in the A(H5) viruses of clade 2.3.4.4b collected in birds in Europe since October 2020. This observation suggests that these mutations with potential public health implications have likely emerged upon transmission to mammals.

HPAI A(H5N1) viruses in cats in Poland

Complete genome sequences of 20 A(H5N1) virus-positive cats collected during the second half of June 2023 from six voivodeships in Poland indicate that the viruses belong to clade 2.3.4.4b, genotype CH (H5N1-A/Eurasian_Wigeon/Netherlands/3/2022-like). These viruses are highly related to each other and cluster with a virus of the same genotype detected at the beginning of June in a white stork (*Ciconia ciconia*) in Poland. This genotype has circulated widely in wild birds in Europe since October 2022 and, it has been responsible for several outbreaks in poultry in Poland, mainly in the Wielkopolskie area, as well as for cases in wild birds between December 2022 and January 2023. However, since February 2023, this genotype has only been sporadically identified in the country.

All the viruses detected in cats possess two mutations in the PB2 protein, E627K and K526R, which are molecular markers of virus adaptation in mammals (Suttie et al., 2019). PB2-E627K has been previously demonstrated to enhance polymerase activity, virus replication, and in certain cases, pathogenicity and mortality in mammals (Subbarao et al., 1993; Hatta et al., 2001; Shinya et al., 2004; Labadie et al., 2006; Salomon et al., 2006; Hatta et al., 2007; Mehle and Doudna, 2008; Fornek et al., 2009; Li et al., 2009; Rameix-Welti et al., 2009; Steel et al., 2009). The same mutation is in the A(H5N1) virus detected in the white stork at the beginning of June. PB2-K526R has been identified in some avian influenza viruses responsible for human cases (H5N1 and H7N9) and in the majority of the



seasonal A(H3N2) human cases (Song et al., 2014). A previous study showed that A(H7N9) viruses possessing both 526R and 627K replicate more efficiently in mammalian (but not avian) cells and in mouse lung tissues and cause greater mortality in infected mice (Kobasa et al., PREPRINT (Version 1)).

To date, the A(H5N1) viruses from Polish cats are the only 2.3.4.4b viruses having both mutations.

2.3 Avian influenza virus infections in humans

2.3.1 Most recent human infections with avian influenza A(H3N8), A(H5N1), A(H5N6) and A(H9N2) viruses

Since 10 May 2023 and as of 4 July 2023, five new human cases or detections with avian influenza infection were reported from the United Kingdom (two cases A(H5N1)) and China (one A(H5N6), two A(H9N2)) (Table 3). All five people had exposure to poultry or live poultry markets prior to detection of avian influenza viruses.

Specifically, China reported one new human infection with A(H5N6) in an adult with critical condition and two new cases of A(H9N2) infection, in two children with mild symptoms in 2023 (CHP, 2023; ECDC, 2023a; WHO, 2023b).

Subtype	New cases reported	Total cases (deaths)	Countries reporting human cases
A(H3N8)	-	3 (1) Since 2022	China
A(H5N1)	TWO new detections in the United Kingdom (asymptomatic workers, one with contamination and second with uncertain level of contamination)	876 (458) Since 2004	23 countries reported cases, EU/EEA: Spain with virus fragment detections in two poultry workers considered contamination and no productive infections
A(H5N6)	ONE new case in China	85 (33) Since 2014	China (84), Laos (1)
A(H9N2)	TWO new cases in China	125 (2) Since 1998	No EU/EEA country; China (109), Egypt (4), Bangladesh (3), Cambodia (2), Oman (1), Pakistan (1), India (1), Senegal (1)

Table 3:	Most recent human ca	ases due to avian influenza	viruses, by virus subtype

Source: ECDC line list and WHO.

2.3.2 Human A(H3N8) cases, summary

Since the previous report and as of 4 July 2023, one previously reported case died, a 56-year-old woman who had underlying conditions (WHO, 2023a). Overall, there have been three human infections with A(H3N8), including one death, all reported from China within 13 months. Two infections were reported in children (4 and 5 years old) and one in



and adult (56-year-old female) exposed to either infected backyard poultry or live poultry markets. The infections were mild in one case and more severe or critical in the other two (Bao et al., 2022; Sit et al., 2022). Human-to-human transmission has not been reported and all three cases were considered sporadic spill-over events.



The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on: 4 July 2023

Figure 9: Geographic distribution of human A(H3N8) cases, 2022–2023 (source: ECDC line list)

2.3.3 Human A(H5N1) cases, summary

As of 23 June 2023, there have been 876 human cases including 458 deaths with A(H5N1) infection notified to WHO from 23 countries (Azerbaijan, Bangladesh, Cambodia, Canada, Chile, China, Djibouti, Ecuador, Egypt, Indonesia, India, Iraq, Laos, Myanmar, Nepal, Nigeria, Pakistan, Spain⁹, Thailand, Türkiye, Vietnam, United Kingdom and United States of America; Figure 10).

In 2022, five countries reported six human cases/detections (Figures 10 and 11): China (1), Ecuador (1), Spain⁹ (2), United States of America (1) and Vietnam (1). In 2023, four countries reported six cases/detections: Cambodia (2), Chile (1), China (1) and the United Kingdom (2).

In 2022, Spain reported the detection of viral A(H5N1) RNA of clade 2.3.4.4b in two asymptomatic poultry farm workers involved in culling activities, but the epidemiological, laboratory and serological analyses confirmed a mucosal contamination (no sequencing

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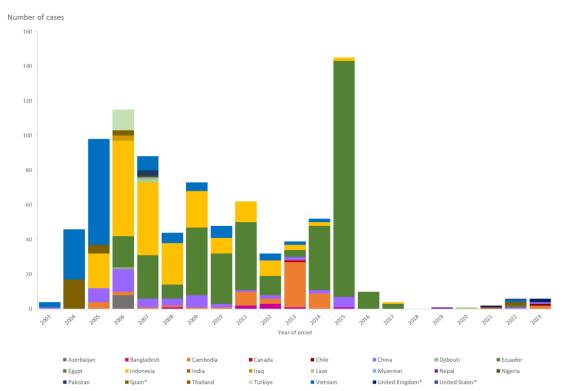
⁹ A(H5N1) detections in two Spanish poultry workers involved in culling activities are considered contaminations and not productive infections.

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possible, no antibodies against H5 and no virus isolation possible) with no demonstrated productive infections.

In 2023, the United Kingdom reported two detections of A(H5N1) of clade 2.3.4.4.b in two individuals who were involved in culling and cleaning activities in a poultry farm affected with confirmed A(H5N1) virus outbreak among birds (GovUK, online-b). According to the same report, one of the individuals is considered to have a contamination and not a true infection, while it remains uncertain if the detection in the second individual is due to an infection or a contamination. The two cases were detected through a surveillance study 'Asymptomatic avian influenza surveillance of poultry workers'. Both individuals tested negative at the end of isolation, and one received treatment with oseltamivir. No serological results are currently available (GovUK, online-b).

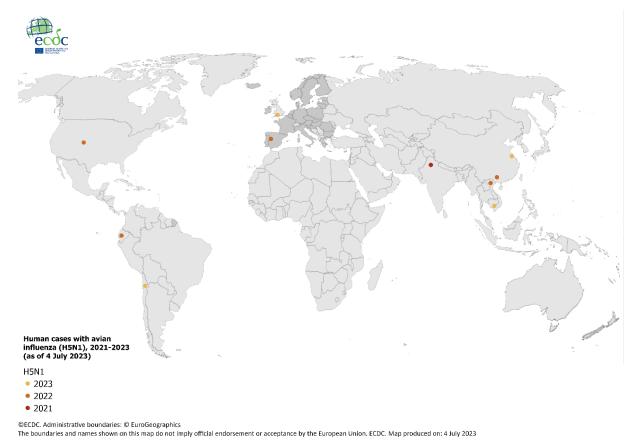


*Note: includes five detections due to suspected environmental contamination and no evidence of infection reported in 2022 from Spain (2) and the United States (1), and in 2023 from the United Kingdom (1).

Figure 10: Distribution of confirmed human cases of HPAI A(H5N1) virus infection by year of onset and country, 2003–2023 (data as of 4 July 2023, n = 876)

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*Note: includes five detections due to suspected environmental contamination and no evidence of infection

reported in 2022 from Spain (2) and the United States (1), and in 2023 from the United Kingdom (1).

Figure 11: Geographic distribution of human A(H5N1) cases, 2021–2023 (source: ECDC line list)

2.3.4 Human A(H5N6) cases, summary

As of 4 July 2023 and since 2014, China (84) and Laos (1) reported a total of 85 human infections with A(H5N6), including 33 (39%) with fatal outcome according to notifications to WHO (Figure 12). Since 2021, the majority of A(H5N6) viruses identified in humans belong to clade 2.3.4.4b, although sequence information is not available for all viruses. After the modification of the H5 component in the vaccine used for poultry in China in January 2022, the number of human cases declined. However, with the available information it is not possible to make any further conclusions on whether the vaccination caused the observed decline (Chen et al., 2022; Cui et al., 2022; Gu et al., 2022; Zhu et al., 2022).



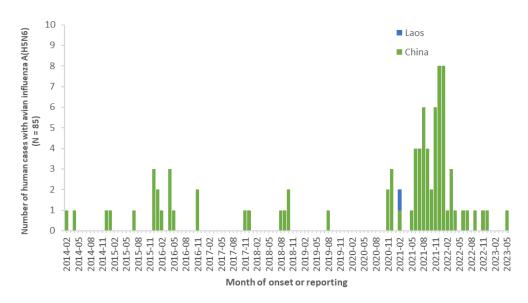


Figure 12: Distribution of confirmed human cases of A(H5N6) virus infection by month and year of onset and country, 2014–2023 (data as of 4 July 2023, n = 85)

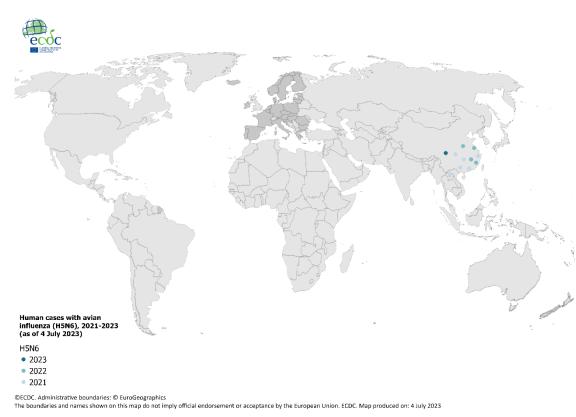


Figure 13: Geographic distribution of human A(H5N6) cases, 2022–2023 (data as of 4 July 2023, n = 85; source: ECDC line list)

2.3.5 Human A(H9N2) cases, summary

As of 4 July 2023 and since 1998, a total of 125 human infections including two fatalities with A(H9N2) have been reported from eight countries all outside the EU (Figure 14): Bangladesh (3), China (112), Cambodia (2), Egypt (4), Pakistan (1), Oman (1), India (1) and Senegal (1) (Figure 12). The majority of infections were identified in children up to 9



years of age (95; 76%) and women were more affected than men (73 vs. 50; 2 of unknown sex).

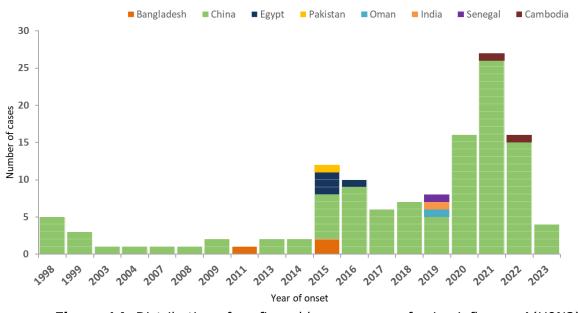


Figure 14: Distribution of confirmed human cases of avian influenza A(H9N2) virus infection by month and year of onset and country, 1998–2023 (as of 4 July 2023, n = 125)

2.3.6 Genetic characteristics of HPAI viruses of the A(H5Nx) subtype from humans

Based on the data available from the GISAID's EpiFlu[™] Database¹⁰, since 2020 human infections have been caused by four different A(H5) clades of the A/goose/Guangdong/1/1996-lineage, namely 2.3.2.1c (Laos, 2020 and Cambodia, 2023), 2.3.2.1a (India, 2021), 2.3.4.4h (China, 2020–2021) and 2.3.4.4b (China, Europe, North America, South America, 2020–2023).

Mutation Q226L was identified in two A(H5N6) viruses of clade 2.3.4.4b collected in China in 2021 (Zhu W Fau - Li et al.). This mutation is associated with the switch in the receptor specificity from avian-type to human-type receptor (Stevens et al., 2006; Chutinimitkul et al.; Russell et al., 2012). This mutation was previously detected in two A(H5N1) viruses of clade 1 collected from human infections in Cambodia in 2013 (Rith et al., 2014) and, based on the available sequence data, it is not present in the clade 2.3.4.4b A(H5Nx) viruses currently circulating in the avian population in Europe. Moreover, six clade 2.3.4.4b A(H5N6) viruses collected from human infections in China in 2021 possessed one of the adaptive markers in the PB2 protein (Q591K, E627K or D701N) associated with an increased virulence and replication in mammals (Zhu W Fau - Li et al., 2022).

Available sequence information from the virus A/Chile/25945/2023 detected from the human case in Chile in March 2023 shows that the 2.3.4.4b clade virus carries two amino acid substitutions in PB2, indicative of mammalian adaptation, Q591K and D701N. Q591K has been associated with increased polymerase activity and replication in mammalian cell lines and increased virulence in mice, while D701N was also associated with increased

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¹⁰ <u>https://gisaid.org/</u>



virulence and contact transmission in guinea pigs (Li et al., 2005; Gao et al., 2009; Le et al., 2009; Steel et al., 2009; Yamada et al., 2010; Taft et al., 2015; Suttie et al., 2019).

There are sequencing data available from the two UK cases from May 2023 (whole genome from the second case and partial genome from the first case). According to the UK technical briefing 4 (GovUK, online-b), the genomes are of clade 2.3.4.4b, with the complete genome being classified as UK genotype AIV48, also known as the A/gull/France/22P015977/2022-like genotype (or BB genotype). Apart from non-synonymous amino acid substitutions and a mutation in NP: S310N, no additional mutations were observed in the sequence data available. Further analyses are ongoing for the assessment of any phenotypic significance of the identified mutations.

2.3.7 Additional information and international risk assessments

A study of currently circulating A(H5N1) viruses in North America showed that these viruses are able to replicate efficiently in human respiratory tract cell types and that in ferret infection and transmission studies, animals got infected but showed only very mild symptoms mostly limited to upper respiratory tract and viruses did not transmit to other ferrets kept in a direct-contact setting (Pulit-Penaloza et al., 2022).

Another study with A(H5N1) viruses from North America belonging to different genotypes demonstrated that viruses are able to replicate in primary human airway epithelial cells (Darwyn Kobasa, 2023). These viruses derived from different wild animal species that died following infection. Moreover, one 2.3.4.4b isolate carrying the PB2-E627K mutation was efficiently transmitted through direct contact between ferrets, resulting in lethal outcomes.

Recently, OFFLU¹¹, a WOAH-FAO network of expertise on animal influenza, published a statement regarding the infections of cats with A(H5N1) in Poland¹².

The previously issued risk assessment using the Influenza Risk Assessment Tool (IRAT) of the United States Centers for Disease Control and Prevention (US CDC) placed the risk of clade 2.3.4.4b viruses in the lower moderate category (CDC, 2021). The risk of the A(H5N1) clade 2.3.4.4b viruses currently circulating in the United States bird and poultry populations, which are closely related to European viruses, was assessed by the US CDC to be low for human health in the general population and higher for people occupationally or recreationally exposed to birds (CDC, online-a, c). An updated IRAT assessment for the A(H5N1) clade 2.3.4.4.b virus from the mink farm outbreak in Spain in 2022 scored slightly higher in some risk elements than the virus of clade 2.3.4.4.b previously assessed overall indicating a comparable `moderate' risk level (CDC, online-b).

The WHO assessed the risk related to the recent A(H5N1) viruses infecting humans as low for the general public and low to moderate for occupationally exposed people (WHO, 2022, online). WHO previously assessed the risk for A(H5N6) as follows: 'the zoonotic threat remains elevated due to spread of the viruses in birds, based on evidence available so far, the overall pandemic risk is considered not significantly changed in comparison to previous years'. The UK Health Security Agency (UKHSA) assesses the situation to remain at level 3 (with limited mammalian transmission that excludes humans but with low confidence) on a scale ranging between 0–6 similar to the previous assessment REF (GovUK, online-c, b, a). A joint EFSA, ECDC and EURL publication from 2021 already

¹¹ https://www.offlu.org/

¹² https://www.offlu.org/wp-content/uploads/2023/06/OFFLU-first-statement-Poland_28June.pdf



described the threat to humans with the objective to raise awareness among clinicians in the EU around zoonotic avian influenza virus infection and consider testing (Adlhoch et al., 2021). Additional information is also available in the Joint ECDC/EFSA/EURL/EU-OSHA document on 'Testing and detection of zoonotic influenza virus infections in humans in the EU/EEA, and occupational safety and health measures for those exposed at work' (ECDC, 2022b).

2.3.8 ECDC risk assessment

Overall, the risk of infection of humans with avian influenza viruses of the currently circulating clade 2.3.4.4b A(H5) virus in Europe for the general public in EU/EEA countries remains low.

The risk to occupationally or otherwise exposed groups to avian influenza infected birds or mammals including infected cats is currently assessed as low to moderate.

Considering the uncertainties regarding the ongoing situation in Poland with confirmed A(H5N1) infections in domesticated cats, this assessment will be continuously reviewed and updated when more information becomes available. Polish public health authorities are monitoring people exposed to A(H5N1) infected cats and no symptomatic person or any human infection has been identified so far. Serological studies are planned to investigate any possibility of asymptomatic transmission.

More information on the methodology used for the assessment of the risk can be found at the published ECDC operational tool on rapid risk assessment methodology (ECDC, 2022a).

Viruses continue to spread and diversify globally. Viruses currently circulating in bird populations in Europe are avian-adapted viruses, e.g. they bind to avian-like receptors, transmit and replicate best in bird species. The viral genotype does not predict the viral phenotype and therefore a high uncertainty is associated with any assessment of the risk for humans, particularly due to the high variability and diversification of the avian influenza viruses of clade 2.3.4.4b with many reassorted subtypes and genetic lineages co-circulating in Europe and globally as well as the sporadic occurrence of various mutations that could increase the transmission to and replication in humans. Reassortment events will likely continue globally leading to a more complex situation.

Mutations associated with mammalian adaptation have been identified sporadically in few birds but emerged more frequently in mammalian hosts after infection. Such mutations were also observed in the virus strains identified in cats in Poland. Despite the occurrence of mutations associated with increased replication in mammalian hosts contributing to mammalian adaptation in viruses infecting mammals as well as sporadically in wild birds and poultry, the viruses analysed retain preferential binding to avian receptors.

Up to now, no mammal-to-human transmission of clade 2.3.4.4b viruses has been observed. In the investigation of infected cats in Poland neither feline-to-feline nor feline-to-human transmission have been identified so far.

Avian influenza transmission from animals to humans is a rare event, nevertheless, transmission to humans cannot be excluded when avian influenza viruses are present in birds, domesticated mammals and other animals, and people are in direct contact without protection. Despite large number of human exposure events to clade 2.3.4.4b viruses in

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EU/EEA over the last three years e.g. exposure to poultry during culling operations or wild bird findings, no symptomatic infection has been identified and reported.

The majority of human cases developing symptoms after infection with clade 2.3.4.4b viruses were reported to have had unprotected exposure to infected sick or dead poultry mostly in backyard settings.

Circulation of clade 2.3.4.4b viruses is continuing in Europe causing infections and deaths in wild birds, wild and domesticated mammals, as well as outbreaks in poultry farms or small holdings such as backyard farms with low biosecurity measures and high environmental contamination with avian influenza viruses are observed. With the presence of avian influenza viruses, sporadic human infections with avian influenza viruses cannot be excluded for people in direct contact with infected sick or dead animals particularly if they are not wearing personal protection equipment. Human infections with severe disease progression and fatal outcomes have been observed outside the EU and such severe infections can also not be excluded should infections in the EU occur.

Based on the analyses of known molecular markers associated with resistance toward antiviral drugs in the available sequences, the majority of the circulating A(H5N1) viruses in Europe, including those detected in cats in Poland, remain susceptible to licensed antivirals for use in seasonal influenza virus infections as well as for pandemic use (neuraminidase inhibitors (oseltamivir, zanamivir), M2 blockers (adamantanes) and cap-dependent endonuclease blocker (baloxavir marboxil). All antivirals are available as treatment options and pre- or post-exposure prophylaxis.

The proposed candidate vaccine viruses prepared for pandemic preparedness (to develop H5 vaccines for humans) are considered to be antigenically similar to the currently circulating clade 2.3.4.4b viruses in Europe. Vaccines against A(H5) viruses for the use in humans are not available at the moment.

Monitoring of avian influenza viruses in birds and mammals including sharing of sequence data is crucial for updated risk assessment and implementation of measures in the animal-human interface.

ECDC recommends virus subtyping of specimens from hospitalised patients with influenza A virus infection. Also patients with unexplained neurological symptoms in hospital setting should be tested for influenza virus to rule out any severe avian influenza virus infection during the summer period where many people could become exposed to dead infected wild birds (ECDC, online).

Interactions with infected animals pose a risk of infection through direct contact (with saliva, nasal secretion or faeces), indirect contact (environmental contamination) or airborne transmission. The susceptibility of cats for A(H5N1) avian influenza viruses is well known (Frymus et al., 2021). The infected cats in Poland as well as the serological evidence of H5 infection in dogs in Italy represent a new and unique exposure situation in Europe, with close and unprotected direct interaction between pets and pet owners taking place. Pet owners might not be aware of and informed about the possibility of an avian influenza virus infection and the related symptoms in pets as well as the potential risk of transmission to themselves and family members. So far, no transmission to humans from infected marmals including pets has been documented for clade 2.3.4.4b viruses and more data are required to assess the risk of infection from infected pets to humans. While the source of infection of the cats in Poland remains unknown with significant uncertainty around the



risk for humans, information about the clinical symptoms in cats and protective measures should be shared with pet owners to increase the awareness. Contact details of veterinarians and other authorities investigating this situation should also be made easily available to pet owners.

Options for response and additional information are available on ECDC webpages: <u>Avian</u> influenza (europa.eu).

3. Conclusions

3.1 Birds

- During this reporting period, a major HPAI A(H5N1) epidemic with many reported outbreaks, most of which were secondary outbreaks, occurred in poultry in Southwest France and affected mostly domestic ducks, in particular the foie gras production system. The dominant farm-to-farm transmission may be the result of an increased farm density and number of at-risk contacts (movements of vehicles and personnel), following restocking events in the affected region.
- The A(H5N1) epidemics observed in poultry in Hungary and France during the last and current reporting periods, respectively, have been controlled and are not continuing.
- Relatively few and only sporadic outbreaks were reported in poultry from other European countries.
- In the coming weeks, only sporadic HPAI outbreaks are expected to occur in poultry in Europe; however, more extensive secondary spread cannot be excluded if outbreaks occurred in high density poultry production areas. Higher temperatures and increased ultraviolet radiation expected during summer will decrease the stability of HPAI viruses and thus help in reducing the environmental contamination.
- Outside Europe, A(H5N1) outbreaks in poultry remained at a similar level as during the previous reporting period.
- Given that A(H5N1) virus is currently circulating widely in breeding colonies of black-headed gulls and other seabird species, and given that the juveniles of these species are currently and in the coming weeks fledging and dispersing from their colony sites, the risk exists that virus will be present more widely in the environment in July and August. Together with the lifting of the housing order for free-range poultry in multiple countries in Europe (e.g. United Kingdom, Netherlands, Germany), the risk for A(H5N1) virus incursion into poultry farms across Europe, especially in countries with affected seabird populations, cannot be considered negligible.
- A(H5N1) virus continues to circulate in breeding colonies of black-headed gulls, affecting now also juvenile birds that have hatched and are fledging, resulting in high mortality. At the same time, as predicted in the last report, the host range has been expanded to other gulls and terns, including Mediterranean gulls, black-legged kittiwakes, common terns and sandwich terns. During this reporting period, compared to the situation observed in 2022, seabird species were not only found



dead along coastlines but also inland. The increasing number of wild bird species involved in the A(H5) epidemic may alter the pattern of virus spread.

- Given the current geographical and temporal pattern of HPAI virus detections in wild birds in Europe and higher numbers compared to the same period in the previous year, it is expected that outbreaks in wild birds will continue to occur during the summer months.
- The recent identification of A(H5N5) viruses of Eurasian origin in Canada and A(H5N1) viruses of African origin along the European Mediterranean coasts indicate an ongoing inter-continental spread of the virus through wild bird migrations.
- The actual number of dead wild birds during mass mortality events is generally underestimated due to the fact that only very few of those involved are tested in diagnostic laboratories. The real magnitude of the population impact that the A(H5N1) virus infection is having in some species of wild birds will have to be carefully evaluated in the coming months and years.
- The A(H5N1) viruses currently circulating in Europe retain a preferential binding for avian-like receptors; however, several mutations associated with increased zoonotic potential have been detected. Their effects on the biological characteristics of the viruses need to be further investigated.

3.2 Mammals

- Wild and domestic carnivores continue to be the most affected mammalian species by HPAI viruses.
- Three new species, the Southern river otter (*Lontra provocax*) in Chile, the South American coati (*Nasua nasua*) in Germany and Uruguay, and the caracal (*Caracal caracal*) in Poland were found infected by HPAI viruses for the first time.
- Mass mortality events in South American sea lions (*Otaria flavescens*) continue to be reported from the Pacific coastline in South America. The detection of HPAI A(H5) in a South American sea lion in Puerto Williams, at the southern tip of South America, raises the concern for further spread of the virus to Antarctica, e.g. by migratory wild birds.
- Five asymptomatic dogs and one cat in an affected backyard poultry farm were found serologically positive for HPAI A(H5N1) in Italy.
- Twenty-four domestic cats and one caracal with clinical signs and mortality reported were found infected with HPAI A(H5N1) virus in nine different voivodeships in Poland. Uncertainties exist around the source of infection, the potential of feline-tofeline and feline-to-human transmission of the specific A(H5N1) virus strain as well as the severity of the disease. Genetic data indicate that the viruses from cats are highly related, however the number of mutations among the viruses from cats reflects two possible scenarios: one in which the cats might have been exposed to multiple sources of infection of highly related viruses, and another one in which a single source of infection was followed by intra-host evolution in each animal. Based on the existing epidemiological data, a possible scenario is feeding HPAI A(H5N1) virus-contaminated raw poultry meat to these cats. The presence of two molecular



markers of virus adaptation to mammals in all the characterised viruses may increase the zoonotic potential of this strain, although no transmission event to exposed pet owners or other exposed people has been observed.

- HPAI A(H5N1) virus-infected pets may become a potential risk for exposure of further animals and pet owners.
- The ongoing and Europe-wide HPAI A(H5N1) epidemic in seabirds represents a risk for marine mammals along the European coastlines, including harbour seals that breed in the international Wadden Sea as well as for wild and domestic carnivores sharing the same habitat.

3.3 Human cases

- A few sporadic human infections with avian influenza A(H3N8), A(H5N1) and A(H9N2) viruses have been reported from different countries globally since the beginning of 2023.
- Severe and fatal infections in humans have so far been mainly related to unprotected exposure to sick and dead poultry, particularly in backyard settings, as well as contaminated environment or exposure to live bird markets.
- Positive cases due to environmental contamination of the respiratory tract with A(H5N1) virus have been reported when testing asymptomatic persons, e.g. as part of enhanced surveillance program of workers exposed to poultry infected with avian influenza A(H5N1).
- No symptomatic human cases have been detected in the EU despite the likely large number of exposure events over the last years.

4. Options for response

4.1 Birds

- Active surveillance in wild birds, especially in those that silently maintain HPAI viruses in the wild (e.g. waterfowl), is indicated to better describe HPAI viruses circulating in wild bird populations constantly throughout the year. Specific wild bird species that may be targeted for this purpose are, among others, ducks (e.g. dabbling ducks) and seabirds (e.g. gulls and terns).
- Species identification remains of utmost importance for the correct interpretation of passive surveillance efforts in wild birds.
- Close monitoring of seabird breeding colonies, including black-headed gulls and sandwich terns, for unusual mortality will allow for the early detection of HPAI viruses and, if appropriate, the removal of carcasses for the reduction of environmental contamination and therefore reduced mortality and transmission to other species.
- Serological surveillance in seabirds, in particular in endangered species, is needed to evaluate the real level of virus circulation in those species as well as their immune protection.



- Preparedness and prevention strategies continue to be priority measures to be implemented, primarily in high density poultry areas. Also, despite lifting of the housing order in many countries, it may be prudent to keep poultry housed in the coming period in geographical regions where HPAI A(H5) virus is present in seabird populations.
- Timely generation and sharing of genome sequence data from avian influenza viruses is of utmost importance to promptly detect the emergence of viruses with mutations associated with increased zoonotic potential, resistance toward antiviral drugs or different antigenic properties, whose biological characteristics should be further evaluated. Genetic data are also instrumental to track the virus spread and identify novel incursions of viruses which may represent a threat for human or animal health.

4.2 Mammals

- Increased passive surveillance of HPAI viruses in wild (e.g. red foxes) and free-roaming domestic carnivores (e.g. cats and dogs) is indicated, especially in areas with extensive HPAI virus spread in the wild bird population (e.g. mass mortality events) and epidemics in poultry to evaluate both the level of virus infections in these species and the risk for emergence and transmission of adapted viruses. Such surveillance efforts should prioritise domestic mammals present in or around HPAI-affected poultry farms and those with possible contact with infected poultry, wild birds or other mammals. The occurrence of mortality and specific clinical signs, such as those described for the HPAI-affected cats in Poland, in these species should be closely monitored. Research activities to investigate the role of asymptomatic mammals in maintaining HPAI viruses and driving their evolutionary dynamics, e.g. by serological surveillance in farmed mammals (particularly American mink and domestic pig), are recommended. Prompt generation and timely sharing of sequence data is highly recommended to promptly identify the emergence of variants with a possible increased zoonotic potential.
- Disease dynamics associated with HPAI virus infection during mass mortality events in mammal species should be thoroughly investigated. Testing a high number of animals and assuring a prompt generation and sharing of viral sequences data are of utmost importance to shed light on the virus origin, evolution and possible transmission between individuals. The latter is also indicated to timely assess the pandemic risk.
- More accurate and timely reporting of HPAI virus detections in mammals is recommended in a way that reliable numbers of infected animals could be used as quantitative information for risk assessment.
- It is recommended to avoid exposure of domestic cats and dogs, and in general carnivore pets, to dead or diseased animals (mammals and birds), and to avoid feeding domestic cats and dogs offal and raw meat from wild or kept birds in areas where mortality in gulls or other potentially HPAI virus-infected animals are reported. Possible measures are keeping dogs on a leash, and confining cats indoors in areas where extensive circulation of HPAI viruses in wild birds has been confirmed.



4.3 Humans

- Awareness should be raised among the general population to prevent exposure to sick or dead seabirds or mammals. Pet owners should also be informed about clinical symptoms in infected pets, protective measures and contact details of veterinarians and other authorities investigating avian influenza virus infections in mammals.
- Appropriate personal protective equipment should be used when in contact with
 potentially infected animals. People should contact a veterinarian if their pet
 develops severe peracute respiratory or neurological symptoms, avoid contact with
 sick or dead animals as well as clean and disinfect potentially contaminated
 surfaces.
- People exposed to sick or dead birds, infected mammals and contaminated environment should be followed-up for 10–14 days after last exposure and tested immediately following the onset of respiratory or any other symptoms to identify transmission events early.
- Testing of pet owners exposed to infected cats or other pets is recommended irrespective of symptoms.
- People developing symptoms 10–14 days after exposure to avian influenza infected animals should self-isolate, wear a surgical mask or FFP2 respirator when in contact with others, and seek medical advice to inform their healthcare provider about the previous exposure and initiate testing.
- Any suspected or confirmed human infection with avian influenza should be reported as early as possible according to the Regulation on cross-border health threats 2022/2071 to the Early Warning and Response System (EWRS) and according to International Health Regulations (IHR).
- Antiviral pre- and post-exposure prophylaxis with antiviral drugs should be considered following national guidelines and a situational risk assessment.
- Specimens from patients with severe influenza type A infection in hospital settings should be subtyped according to the ECDC guidance on 'Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA' (ECDC, 2023b).
- Patients with viral encephalitis of unknown aetiology should be tested for influenza type A viruses, and specimens should be subtyped if positive to identify potential sporadic infections with similar clinical picture to that observed in infected mammalian species.
- Samples positive for influenza type A virus but negative for A(H1N1)pdm09 or A(H3N2) should be immediately sent to the national influenza reference laboratories for further analysis and subtyping, including H5.



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Appendix A – Terms of Reference

A.1. Background and Terms of Reference as provided by the requestor

Avian influenza is an infectious viral disease in birds, including domestic poultry. Infections with avian influenza viruses in poultry cause two main forms of that disease that are distinguished by their virulence. The low pathogenic (LPAI) form generally only causes mild symptoms, while the highly pathogenic (HPAI) form results in very high mortality rates in most poultry species. That disease may have a severe impact on the profitability of poultry farming.

Avian influenza is mainly found in birds, but under certain circumstances infections can also occur in humans even though the risk is generally very low.

More than a decade ago, it was discovered that virus acquired the capability to be carried by wild birds over long distances. This occurred for the HPAI of the subtype A(H5N1) from South East and Far East Asia to other parts of Asia, Europe and Africa as well as to North America. In the current epidemic the extent of the wild bird involvement in the epidemiology of the disease is exceptional.

Since late October 2016 up to early February 2017, highly pathogenic avian influenza (HPAI) of the subtype A(H5N8) has been detected in wild migratory birds or captive birds on the territory of 21 Member States, namely Austria, Belgium, Bulgaria, Croatia, Czechia, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom. In 17 Member States the virus has spilled over to poultry holdings leading also to lateral spread between holdings in a few Member States, in particular in those with a high density of duck and geese holdings where the poultry cannot sufficiently be protected against contacts with wild birds. A second HPAI subtype A(H5N5) has been detected in wild birds and recently also in poultry holdings in Germany.

The number of infected migratory wild birds found dead and the geographic extent of these findings are posing an immense threat for virus introduction into poultry or captive birds holdings as demonstrated by the high number of outbreaks (~700 as of 08/02/2017).

In the event of an outbreak of avian influenza, there is a risk that the disease agent might spread to other holdings where poultry or other captive birds are kept. As a result, it may spread from one Member State to other Member States or to third countries through trade in live birds or their products.

There is knowledge, legislation, technical and financial tools in the EU to effectively deal with outbreaks of avian influenza in poultry and captive birds. However, the very wide virus spread by wild birds and the increased risk of direct or indirect virus introduction into poultry or captive bird holdings has led to the largest HPAI epidemic in the EU so far. This situation calls for a reflection and evaluation how preparedness, risk assessment, early detection and control measures could be improved.

The Commission and Member States are therefore in need of an epidemiological analysis based on the data collected from the disease affected Member States. The use of the EFSA Data Collection Framework is encouraged given it promotes the harmonisation



of data collection. Any data that is available from neighbouring third countries should be used as well, if relevant.

Therefore, in the context of Article 31 of Regulation (EC) No. 178/2002¹³, EFSA should provide the technical and scientific assistance to the Commission based on the following Terms of Reference (TOR):

- 1) Analyse the epidemiological data on highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI), where co-circulating or linked within the same epidemic, from HPAI disease affected Member States.
- 2) Analyse the temporal and spatial pattern of HPAI and LPAI as appropriate in poultry, captive birds and wild birds, as well the risk factors involved in the occurrence, spread and persistence of the HPAI virus in and at the interface of these avian populations.
- 3) Based on the findings from the points above, describe the effect of prevention and control measures.
- 4) Provide for regular quarterly reports updating on the avian influenza situation within the Union and worldwide, in particular with a view to describe the evolution of virus spread from certain regions towards the EU. In case of significant changes in the epidemiology of avian influenza, these reports could be needed more frequently. These reports should in particular closely follow the developments of zoonotic avian influenza viruses (such as HPAI A(H5N6) and LPAI A(H7N9)) in collaboration with the European Centre for Disease Prevention and Control (ECDC).

A.2 Interpretation of the Terms of Reference

In reply to ToR 1 and ToR 2, this scientific report gives an overview of the HPAI and LPAI outbreaks in poultry, captive and wild birds detected in Europe from 29 April to 23 June 2023 and reported by Member States and neighbouring countries to the ADIS or WOAH. Member States where avian influenza outbreaks have occurred in poultry have submitted additional epidemiological data to EFSA, that have been used to analyse the characteristics of the affected poultry establishments.

It was not possible to collect data for a risk factor analysis on the occurrence and persistence of HPAI virus within the EU. Risk factor analysis requires not only case-related information, but also data on the susceptible population (e.g. location of establishments, population structure), which should be collected in a harmonised manner across the EU. Limitations in data collection, reporting and analysis were explained in the first avian influenza overview report (EFSA et al., 2017).

If HPAI outbreaks in poultry are detected in the EU, a description of the applied prevention and control measures (ToR 3) is given in the overview document provided by representatives from the affected Member States and is provided in <u>Annex A</u>. Information was collected for outbreaks that occurred from 3 April to 9 June 2023. The main topics covered are increasing awareness, release and repeal of housing orders, strengthening

¹³ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, pp. 1–24.



biosecurity, preventive culling, implementation of a regional standstill, bans on hunting and derogations from restriction zone implementation after a risk assessment.

Monitoring of the avian influenza situation in other countries (ToR 4) is based on data reported to WOAH. The description focuses only on findings of avian influenza viruses occurring in countries that are considered to be of epidemiological interest for the EU/EEA and the UK or of public health relevance, specifically on HPAI A(H5N1), HPAI A(H5N2), HPAI A(H5N5), HPAI A(H5N6), HPAI A(H5N8), HPAI/LPAI A(H7N9) and LPAI A(H9N2). The background and epidemiology, detections, phenotypic and genetic characterisations are described based on information from confirmed human, poultry and wild bird cases that occurred from 29 April to 23 June 2023. Possible actions for preparedness in the EU are discussed.

This report mainly describes information that has become available since the publication of the EFSA report for the period March to April 2023 (EFSA et al. 2023b) and that might affect the interpretation of risks related to avian influenza introduction and/or spread in Europe.



Appendix B – Data and Methodologies

B.1 Data on animals

B.1.1 Overview of avian influenza outbreaks in Europe (ToR 1 and ToR 2)

Data on the avian influenza outbreaks that occurred in Europe from 29 April to 23 June 2023 submitted by Member States to the ADIS (European Commission, online) were taken into account for this report. Data extraction was carried on 23 June 2023. WOAH-WAHIS ((WOAH, online-d) was consulted to complement the information for European countries not reporting HPAI notifications to ADIS. In addition, HPAI-affected European countries were asked to provide more detailed epidemiological data directly to EFSA on the avian influenza outbreaks that occurred in poultry up to 9 June 2023. Wild bird species have been categorised according to Table A.3 in Annex A, and the common and scientific names of wild bird species described in this report in relation to Europe are reported in Table A.4 in Annex A. The public GISAID's EpiFluTM Database was accessed to download newly released avian influenza virus sequences.

The annexes to this Scientific Report are available on the EFSA Knowledge Junction community on Zenodo at: <u>https://doi.org/10.5281/zenodo.8133701</u>

B.1.2 Overview of avian influenza outbreaks in other countries not reporting via ADIS (ToR 4)

Data from WOAH-WAHIS (WOAH, online-d) on HPAI A(H5N1), A(H5N2), A(H5N5), A(H5N6), A(H5N8) and LPAI A(H7N9) in domestic and wild birds were used to describe and map the geographic distribution of avian influenza virus detections in domestic and wild birds in Africa, the Americas, Asia and Europe based on the observation dates. Data were retrieved on 29 June 2023 and extracted by EFSA. They were used and reproduced with permission. WOAH bears no responsibility for the integrity or accuracy of the data contained herein, but not limited to, any deletion, manipulation, or reformatting of data that may have occurred beyond its control.

B.1.2 Genetic characterisation of avian influenza viruses: description of the nomenclature of the HPAI A(H5) viruses used in the document

The HA gene of clade 2.3.4.4 A(H5) viruses has rapidly evolved since the most recent official update of the nomenclature of the A/goose/Guangdong/1/1996-lineage H5Nx virus (Smith et al., 2015). This clade emerged in China in 2008 and since then it has acquired various neuraminidase subtypes, including N1, N2, N3, N4, N5, N6 and N8, by reassortments with other avian influenza viruses from different regions, and has evolved into several subgroups. While a revised nomenclature of clade 2.3.4.4 viruses is pending, in previous reports we used the genetic clustering described in 2018 by Lee and co-authors, who recognised four groups (a–d) within clade 2.3.4.4 (Lee et al., 2018). Recently, an update to the unified nomenclature for clade 2.3.4.4 A(H5) viruses has been proposed by the WHO (WHO, 2020) and eight genetic groups (a–h) have been recognised. To align the nomenclature system between international organisations this classification has been adopted for this report. Based on this proposed clustering, A(H5) viruses of clades 2.3.4.4c have spread globally through wild bird migrations during 2014–2015 (2.3.4.4c) and from 2016 to the present day (2.3.4.4b). A list with the distribution of the different genetic



clades reported by countries globally from birds, humans and the environment has been published by WHO in February 2023 (WHO, 2023c).

B.2 Data on humans

The numbers of human cases caused by infection with avian influenza viruses were collected by ECDC. Multiple sources are scanned regularly as part of Epidemic Intelligence activities at ECDC to collect information on laboratory-confirmed human cases. Data were extracted and line lists developed to collect case-based information on virus type, date of disease onset, country of reporting, country of exposure, sex, age, exposure, clinical information (hospitalisation, severity) and outcome. All cases included in the line list and mentioned in the document have been laboratory-confirmed. Data are continuously checked for double entries and validity. The data on human cases cover the full period of time since the first human case was reported. Therefore, data on human cases refer to different time periods and are included irrespective of whether there have been any new human cases during the reporting period.